

**Serial No.: 09/787,016**  
**Second Preliminary Amendment**  
**Page 5**

**REMARKS**

With entry of this amendment, Claims 31-61 are pending. Claims 33, 36, 39, 53-59 have been amended. The amendments to the claims have been made to correct minor typographical errors. No new matter has been added by these amendments.

**MARKED COPY OF AMENDMENTS**

**Amendments to the Specification:**

At line 6, page 1, please insert the following paragraph:

This application is filed under 35 U.S.C. §371 as the U.S. national stage application of International Application No. PCT/GB99/03019 filed September 10, 1999. This application additionally claims benefit of U.S. Provisional Application No. 60/100,973 filed September 17, 1998. This application also claims benefit of Swedish Application No. 0903069-5 filed September 10, 1999.

**Amendments to the Claims:**

Please amend the claims as follows:

33. (Amended) An isolated DNA [the nucleotide sequence] comprising SEQ ID NO: 3 and variants and alleles thereof that codes for expression of the murine [Death Inducer-Obliterator 1] DIO-1 Gene.

36. (Amended) The isolated DNA of Claim\_33, comprising a fragment comprising an N-terminal domain, a central non-canonical Zn finger domain. and a C-terminus domain containing a K-rich region.

39. (Amended) An isolated DIO-1 polypeptide derived from the DNA sequence SEQ ID NO: 3 and variants and alleles thereof.

49. (Amended) A method for identifying clones encoding a DIO-1 polypeptide of SEQ ID NO: 2, or SEQ ID [No] NO: 4, comprising screening a genomic or cDNA library with

a nucleic acid probe according to [claim] Claim 41 [10] under low stringency hybridization conditions, and identifying those clones which display a substantial degree of hybridization to said probe.

53. (Amended) A method to produce specific monoclonal and polyclonal antibodies against the polypeptide encoded by [according to claims] SEQ ID NO: 2[,] or SEQ ID NO: 4 comprising the injection [infection] of the polypeptide [to] into a [mammalian] mammal.

54. (Amended) A method [Method] for treatment of diseases which are characterized by the alteration in cell death or by hyperproliferation, comprising, administering [characterized by the administration of] compounds encoded by [according to] SEQ ID NO: 2[,] or SEQ ID NO: 4, or agonists or antagonists to SEQ ID NO: 2[,] or SEQ ID NO: 4.

55. (Amended) The method [Method according to] of Claim 54, comprising, administering [by administration of] a therapeutically effective amount of the compound.

56. (Amended) The method [Method] according to Claim 54, in which the disease is cancer, an auto[ ]immune disease, diabetes, rheumatoid arthritis, benign and malignant tumors or hyperproliferative skin disorders.

57. (Amended) A method [Method] for treatment of diseases which are characterized in the alteration in cell death or by hyperproliferation, comprising, introducing into a mammal a nucleic acid vector according to Claim 44 and wherein said nucleic acid vector is capable of transforming a cell in vivo and expressing said polypeptide in said transformed cell.

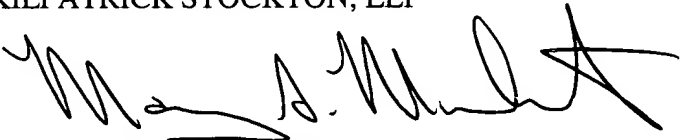
59. (Amended) A method for identifying a ligand to [the compound according to] SEQ ID NO: 2, or SEQ ID NO: 4, or agonists or antagonists to SEQ ID NO: 2, or SEQ ID NO: 4, comprising screening for an agonist or an antagonist of the polypeptide signal transduction to be used for treating metabolic, proliferative or inflammatory conditions.

Serial No.: 09/787,016  
Second Preliminary Amendment  
Page 9

In light of the amendments, Applicants are of the opinion that the application is now in condition for allowance. Such action is respectfully requested. If the Examiner believes any informalities remain in the application which may be corrected by Examiner's Amendment, or there are any other issues that can be resolved by telephone interview a telephone call to the undersigned attorney at (404) 815-6500 is respectfully solicited.

Respectfully submitted,

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